Tetrahedron 67 (2011) 334–338

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Acetyl-BINOL as mimic for chiral β-diketonates: a building block for new modular ligands

Robert von Rönn, Jens Christoffers *

Institut für Reine und Angewandte Chemie, Carl von Ossietzky-Universität Oldenburg, D-26111 Oldenburg, Germany

ARTICLE INFO

Article history:
Received 5 October 2010
Received in revised form 5 November 2010
Accepted 8 November 2010
Available online 13 November 2010

Keywords:
Homogeneous catalysis
Chiral ligands
BINOL derivatives
Asymmetric catalysis
Titanium
Amino acid derivatives

ABSTRACT

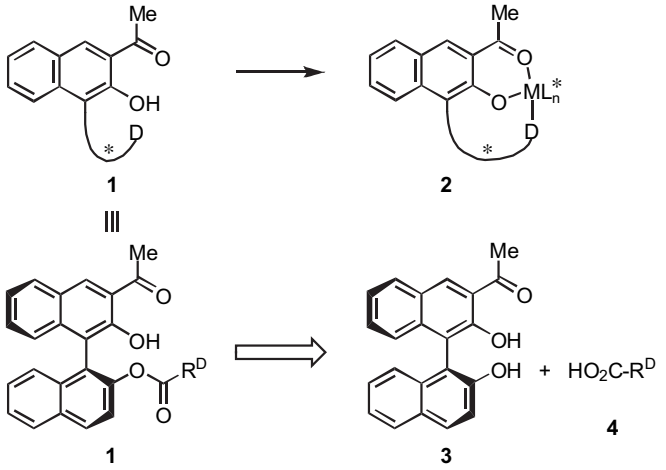
α-Acetyl-(*S*)-BINOL was prepared by *ortho*-lithiation and subsequent acetylation of acetal-protected (*S*)-BINOL. The β-hydroxyketone moiety of this compound is herein a structural mimic for a β-diketonate and forms six-membered chelates with transition metal ions. The second hydroxy-function was submitted to esterification with several carboxylic acids bearing another donor function, thus, new tridentate chiral ligands were obtained. Out of this library the L-proline-α-acetyl-(*S*)-BINOL-ester was identified to be most effective for the titanium-mediated addition of Et_2Zn to PhCHO yielding the respective secondary alcohol with up to 93% ee, which is better than with using (*S*)-BINOL itself. Besides a solvent dependency (use of MeCN is optimal), the proper choice of the counter-ion is crucial: anion exchange of bromide by trifluoroacetate gave a significant increase of enantioselectivity.

© 2010 Elsevier Ltd. All rights reserved.

1. Introduction

Transition metal β-diketonato complexes are an important class of compounds in homogeneous catalysis.[1] However, chiral cogeners were extraordinarily seldom reported,[2] although they might be of great interest for asymmetric catalysis. The reason for rare reports on such chiral ligands might be, that stereogenic elements can only be implemented at the periphery of the planar six-membered chelates, making effective stereoinduction close to the catalytically active metal center difficult. We envisioned the α-carbonyl phenolate motif to be a reasonable structural mimic for β-diketonate ligands. With an additional donor function D another chelate ring could form and such a ligand **1** would become tridentate and capable of coordination to one face in an octahedral or tetrahedral metal complex **2** (Scheme 1). While the initial stereogenic element is the chiral axis, this second chelate ring would transfer the stereoinformation from the periphery of the acylphenol **1** to the metal fragment ML_n, thus, the metal center itself is becoming a stereocenter. With additional coordination sites L_n, the stereogenic metal center might be able to catalyze suitable C–C bond forming reactions in an asymmetric fashion.

We considered 3-acetyl-2,2′-dihydroxy-1,1′-binaphthyl (**3**) to be a suitable scaffold for such tripodal ligands **1**, since it combines all three key features of our new ligand concept: first, the 2-OH and the 3-acetyl group are a perfect mimic of a β-diketone, as already indicated by intramolecular H-bonding. Secondly, the other 2′-OH group is suitable for esterification with various carboxylic acids **4**, which carry the additional donor function D. Third, the chiral axis directs the chelating group D above the planar β-hydroxycarbonyl moiety of this scaffold, thus, providing the prerequisite for facial coordination to an octahedral or tetrahedral metal center. Since the



Scheme 1. A library of modular α-acetyl-BINOL derivatives **1** with additional donor functions D as mimetics of chiral β-diketonato complexes **2** and their synthesis from (*S*)-α-acetyl-BINOL (**3**) and carboxylic acids **4**.

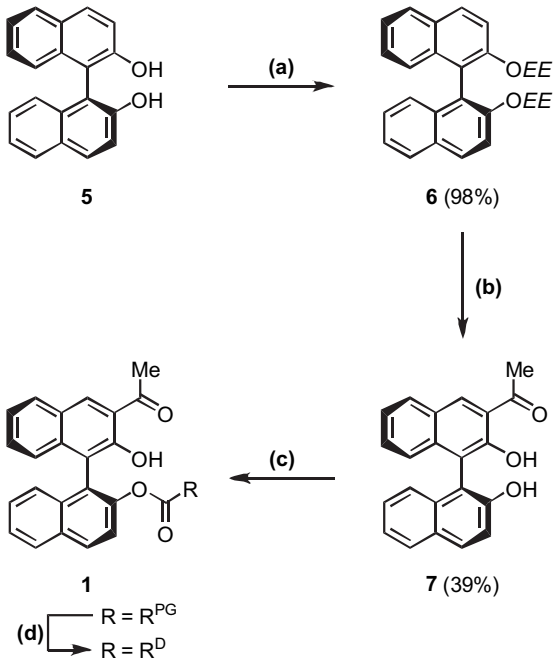
* Corresponding author. Tel.: +49 441 798 4744; fax: +49 441 798 3873; e-mail address: jens.christoffers@uni-oldenburg.de (J. Christoffers).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.11.037

BINOL moiety is a leading structure in asymmetric catalysis,[3] it is not surprising that tridentate BINOL derivatives have been successfully prepared and applied before.[4] However, respective compounds with a β-diketone mimicking motif have never been reported. For this reason, we wish to report herein on the synthesis of ligands **1** with a different range of donor groups D. We moreover report on the application of these ligands in a well investigated model reaction:[5] the titanium catalyzed nucleophilic addition of Et_2Zn to benzaldehyde. This process can be realized with BINOL itself with high yields and selectivities.[6]

2. Results and discussion

For the synthesis of ligand library **1** we envisioned introduction of the acetyl group after *ortho*-metalation. For this purpose, the ethoxyethyl (EE) protective group seemed to be a suitable acetal function for directing the metalation.[7] Twofold EE-protection of (*S*)-BINOL (**5**) proceeded as reported earlier by others (Scheme 2, 98% yield).[8] *ortho*-Deprotonation of bisacetal **6** underwent smoothly with a small excess of *n*-BuLi, however, conversion with different acetylating reagents turned out to be very tedious. For example, methyl acetate gave only traces of product **7**, although we had good experience with it in another project.[9] The application of AcCl, $AcNMe_2$, AcCN or MeCHO (with subsequent oxidation) neither gave significant amounts of compound **7**. Finally, the application of excess Ac_2O followed by acidic workup in order to cleave the acetal protective groups furnished α-acetyl-BINOL **7** as a yellow solid. The esterification as diversifying synthetic step was performed with carboxylic acids **4** and DCC as coupling reagent in the presence of catalytic amounts of DMAP. This esterification was first of all explored with the conversion of $PhCO_2H$ (**4a**). To our delight, it proceeded completely regioselective, as it is indicated by the chemical shifts of OH groups in the NMR spectra: compound **7** has the signal of the 2-OH-proton at 12 ppm, because it is involved in H-bonding to the 3-acetyl group. The phenolic 2′-OH appears at 5 ppm. The signal of the acidic proton of compound **1a** (and later on in all other examples **1b**–**1w**) shows up at 12 ppm, again clearly indicating H-bonding to the adjacent carbonyl group. Table 1 lists carboxylic acids **4** as well as yields of corresponding esters **1**. Several benzoic acid derivatives (**4b**–**4h**, entries 2–8) as well as picolinic (**4i**, entry 9) and nicotinic acids (**4j**, entry 10) were applied. Moreover, derivatives of L- and D-proline (**4k**–**4l**, entries 11 and 12) and L-valine (**4m**, entry 13) were submitted to esterification. In these and some other cases the donor function D of residues R^D needed protection in order to perform the esterification step. Other carboxylic acids with protected residues R^{PG} were compounds **4c**, **4d**, **4f**, and **4g**, which were debenzylated subsequently to the esterification step. Table 2 lists deprotection conditions and yields. For anthranilic acid **4e** and valine **4m** the *N*-Boc protective group was used, whose cleavage was unproblematic when performed with TFA (entries 3 and 10). Actually, we used *N*-Boc-L-proline instead of **4k** in initial experiments. It however turned out that Boc-deprotection with TFA did not give the corresponding ester **1t**. For unknown reasons, decomposition under formation of compound **7** occurred. Therefore, Cbz was chosen as the protective group for proline. The Cbz-group was then cleaved with HBr[10] and the hydrobromides **1s** and **1u** (entries 6 and 8) were formed. In subsequent studies a significant anion dependence of enantioselectivities was observed (vide infra). For this reason, the bromide was exchanged by trifluoroacetate (ligands **1t** and **1v**, entries 7 and 9). This anion change was achieved by evaporating the pyrrolidinium bromide with TFA. Conversion was monitored by ESI-MS (negative mode); it was complete when no more bromide was detectable.



Scheme 2. Synthesis of library of modular α-acetyl-BINOL derivatives **1** with additional donor functions D. Reagents and conditions: (a) 4 equiv EVE, 0.1 equiv PPTS, CH_2Cl_2, 23 °C, 16 h; (b) 1. 1.2 equiv *n*-BuLi, THF, 0 °C, 15 min; 2. 10 equiv Ac_2O, 0 °C, 15 min, 23 °C, 15 min; 3. HCl–H_2O, 23 °C, 30 min; (c) 1 equiv RCO_2H **4**, 1.2 equiv DCC, 0.1 equiv DMAP, CH_2Cl_2, 60 °C, 16 h; for residues R (R^D or R^{PG}) and yields see Table 1; (d) for deprotection details and conditions see Table 2; EVE=ethylvinylether, PPTS=pyridinium *para*-toluenesulfonate, DCC=dicyclohexylcarbodiimide, DMAP=4-(dimethylamino)pyridine, EE=1-ethoxyethyl.

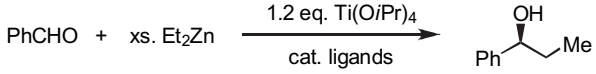
Table 1
Esterification of acetyl-BINOL **7** with carboxylic acids **4**. Compounds **1c**–**1g** and **1k**–**1m** were subsequently deprotected (see Table 2)

Entry	RCO_2H	Product	Yield (%)
1	$PhCO_2H$ **4a**	**1a**	74
2	2-$MeOC_6H_4CO_2H$ **4b**	**1b**	53
3	2-$BnOC_6H_4CO_2H$ **4c**	**1c**	61
4	3-$BnOC_6H_4CO_2H$ **4d**	**1d**	51
5	2-$BocHNC_6H_4CO_2H$ **4e**	**1e**	41
6	2-$BnO_2CC_6H_4CO_2H$ **4f**	**1f**	49
7	3-$BnO_2CC_6H_4CO_2H$ **4g**	**1g**	68
8	2-$Ph_2PC_6H_4CO_2H$ **4h**	**1h**	64
9	2-Pyridyl-CO_2H **4i**	**1i**	65
10	3-Pyridyl-CO_2H **4j**	**1j**	64
11	(*S*)-*N*-Cbz-proline **4k**	**1k**	83
12	(*R*)-*N*-Cbz-proline **4l**	**1l**	49
13	(*S*)-*N*-Boc-valine **4m**	**1m**	64

In order to establish the feasibility of our new ligand library, we adopted a procedure for a titanium-mediated asymmetric addition of Et_2Zn to benzaldehyde as reported by Mori and Nakai,[6] who converted PhCHO with Et_2Zn in the presence of 1.2 equiv $Ti(O\textit{i}\text{-}Pr)_4$ and 0.1 equiv (*S*)-BINOL and achieved 85% ee of (*S*)-1-phenyl-1-propanol (Scheme 3). First of all, we used (*S*)-BINOL (**5**) itself in order to check our procedure and to compare it with Mori's results. With this experiment, we furthermore established a reference for the absolute configuration of the product. Conversion as well as enantiopurity of the product was determined by GLC on a chiral phase after quenching a sample of the reaction mixture with aqueous NH_4Cl. In order to compare reaction rates with different ligands, we stopped every batch after 1 h stirring at 0 °C and listed the respective conversion in the Tables 3–5. Quantitative conversions could of course be achieved in all cases when running the reactions over night. The control experiment with (*S*)-BINOL (**5**) resulted in 78% conversion and 81% ee (Table 3, entry 1). Next we checked the effect of acetyl-BINOL **7**, which gave lower ee than BINOL (entry 2). Furthermore, benzoic ester **1a** without a third

Table 2
Deprotection and anion exchange

Entry	Educt	R^D	Deprotection conditions	Product	Yield (%)
1	**1c**	2-C_6H_4OH	1 bar H_2, cat. Pd/C, EA, 23 °C, 4 h	**1n**	58
2	**1d**	3-C_6H_4OH	1 bar H_2, cat. Pd/C, EA, 23 °C, 28 h	**1o**	81
3	**1e**	2-$C_6H_4NH_2$	TFA, CH_2Cl_2, 23 °C, 20 h	**1p**	63
4	**1f**	2-$C_6H_4CO_2H$	1 bar H_2, cat. Pd/C, EA, 23 °C, 3 h	**1q**	86
5	**1g**	3-$C_6H_4CO_2H$	1 bar H_2, cat. Pd/C, EA, 23 °C, 6 h	**1r**	73
6	**1k**	(*S*)-2-Pyrrolidinium bromide	HBr/AcOH, 23 °C, 45 min	**1s**	88
7	**1s**	(*S*)-2-Pyrrolidinium trifluoroacetate	TFA, 23 °C, 12 h	**1t**	89
8	**1l**	(*R*)-2-Pyrrolidinium bromide	HBr/AcOH, 23 °C, 45 min	**1u**	79
9	**1u**	(*R*)-2-Pyrrolidinium trifluoroacetate	TFA, 23 °C, 12 h	**1v**	85
10	**1m**	(*S*)-*i*-PrCHNH_2	TFA, CH_2Cl_2, 23 °C, 20 h	**1w**	85



Scheme 3. Screening reaction; for conditions see Tables 3–5.

Table 3
First screening. Conditions: 1 equiv PhCHO, 3 equiv Et_2Zn, 1.2 equiv Ti(O*i*-Pr)$_4$, 0.1 equiv ligand **1**, toluene, 30 min at −78 °C, then 1 h at 0 °C

Entry	Ligand	R^D	Conv. (%)	ee[a] (%)
1	**5**	—	78	81
2	**7**	—	75	60
3	**1a**	Ph	65	0
4	**1b**	2-C_6H_4OMe	68	58
5	**1h**	2-$C_6H_4PPh_2$	79	44
6	**1i**	2-Pyridyl	90	65
7	**1j**	3-Pyridyl	56	0
8	**1n**	2-C_6H_4OH	48	23
9	**1o**	3-C_6H_4OH	96	0
10	**1p**	2-$C_6H_4NH_2$	35	0
11	**1q**	2-$C_6H_4CO_2H$	70	43
12	**1r**	3-$C_6H_4CO_2H$	80	10
13	**1s**	(*S*)-2-Pyrrolidinium bromide	41	75
14	**1t**	(*S*)-2-Pyrrolidinium trifluoroacetate	66	84
15	**1w**	(*S*)-*i*-PrCHNH_2	90	69

[a] In all cases with ee>0% the major isomer is (*S*)-1-phenyl-1-propanol.[6]

Table 4
Second screening. Conditions: 1 equiv PhCHO, 2 equiv Et_2Zn, 1.2 equiv Ti(O*i*-Pr)$_4$, 0.15 equiv ligand **1**, MeCN, 30 min at −40 °C, then 1 h at 0 °C

Entry	Ligand	R^D	Conv. (%)	ee[a] (%)
1	**1s**	(*S*)-2-Pyrrolidinium bromide	36	85
2	**1t**	(*S*)-2-Pyrrolidinium trifluoroacetate	75	93
3	**1u**	(*R*)-2-Pyrrolidinium bromide	35	81
4	**1v**	(*R*)-2-Pyrrolidinium trifluoroacetate	64	78
5	**1t**	(*S*)-2-Pyrrolidinium trifluoroacetate	51	73[b]
6	**1t**	(*S*)-2-Pyrrolidinium trifluoroacetate	80[a]	40[c]

[a] Major isomer is (*S*)-1-phenyl-1-propanol.
[b] CH_2Cl_2 as solvent.
[c] Cyclohexane as solvent.

Table 5
Other substrates with ligand **1t**. Conditions: 1 equiv aldehyde, 2 equiv Et_2Zn, 1.2 equiv Ti(O*i*-Pr)$_4$, 0.15 equiv ligand **1**, MeCN, 30 min at −40 °C, then 1 h at 0 °C

Entry	Aldehyde	Conv. (%)	ee[a] (%)
1	4-$MeOC_6H_4CHO$[12]	39	93
2	2-MeC_6H_4CHO[13]	70	86
3	2-$O_2NC_6H_4CHO$[14]	24	0
4	4-$F_3CC_6H_4CHO$[15]	56	63
5	CyCHO[12b]	40	0

[a] We assume (*S*)-configuration for all three optically active alcohols, since the order of enantiomers in GLC on the chiral phase is the same as for (*S*)-enriched 1-phenyl-1-propanol.

donor function R^D gave racemic product (entry 3). Application of ligand with an *ortho*-donor function R^D=OMe (**1b**, entry 4), PPh_2 (**1h**, entry 5), CO_2H (**1q**, entry 11) as well as 2-pyridyl (**1i**) gave moderate enantioselectivities of 43–65% ee. With *ortho*-R^D=OH (**1n**, entry 8), and NH_2 (**1p**, entry 10) and *meta*-R^D=CO_2H (**1r**, entry 12), OH (**1o**, entry 9) and 3-pyridyl (**1j**, entry 7) low (10–23% ee) or even zero enantioselectivities were achieved. In contrast and to our delight, proline and valine esters **1s** (entry 13) and **1w** (entry 15) gave 75% ee and 69% ee, respectively. We had used the proline-derivative **1s** as the hydrobromide-salt, which was in contrast to our initial plans to use and deprotect an *N*-Boc group. Since we were assuming a significant counter-ion effect, we have prepared the trifluoroacetate **1t** by anion exchange from **1s**. And indeed, the selectivity achieved with this salt **1t** (85% ee) is higher than we observed with (*S*)-BINOL. It is noteworthy to mention that the mode of coordination must now be significantly different from that of BINOL. We suggest tridentate coordination as already indicated in structure **2** (Scheme 1), but this has been not proven so far.

As reported already by others, the solvents can have a significant impact on the selectivity achieved in the reaction shown in Scheme 3. In particular CH_2Cl_2 has been reported to have a beneficial influence.[11] With THF, a racemate was formed, which can be explained by the good coordinating properties of the solvent in competition with the ligand. In cyclohexane and CH_2Cl_2 the ligand **1t** gave lower selectivities compared to results achieved with toluene (Table 4, entries 5 and 6). However, use of MeCN, which was to the best of our knowledge never been reported for the Ti-mediated addition of Et_2Zn to PhCHO, gave again increased optical purity of the product (93% ee, entry 2). Since ligand **1t** has two stereogenic elements, we prepared the diastereoisomer **1v** starting from (*S*)-BINOL (**5**) and *N*-Cbz-(*R*)-proline (**4l**, Table 1, entry 12 and Table 2, entries 8 and 9). This (*S*,*R*)-configuration of ligand **1v** seems to represent the mismatch situation, since the selectivity in MeCN is lower (78% ee) than for the (*S*,*S*)-ligand **1t**. For comparison, results achieved with the hydrobromides **1s** and **1u** in MeCN are also listed in Table 4.

Finally, we adopted our optimized conditions from Table 4 with ligand **1t** to other aldehydes. Electron rich *para*-methoxybenzaldehyde (Table 5, entry 1) gave the same enantioselectivity (93% ee), but reacted significantly slower (only 39% conversion within 1 h at 0 °C). An *ortho*-methyl group did not significantly slow down the reaction (70% conversion), but the enantioselectivity decended below 90% (entry 2). A *para*-nitro-function seemed not to be compatible with our reaction conditions (entry 3). The CF_3-group lowered both, the reaction rate (56% conversion, entry 4) as well as the enantioselectivity (63% ee). Finally, aliphatic cyclohexane carbaldehyde gave low conversion and the product was formed as the racemate (entry 5).

In summary, we reported on a new concept for chiral tridentate ligands **1** based on α-acetyl-BINOL (**7**). The β-hydroxyketone moiety is herein a structural mimic for a β-diketonate. The second hydroxy group allows for modular attachment of another coordinating donor group, which transfers the stereogenic axis to the

metal center. Several examples for this ligand type have been prepared and tested in a model reaction: the titanium-mediated formation of 1-phenyl-1-propanol from PhCHO and Et_2Zn. We were able to identify two members of our ligand library, the L-proline-α-acetyl-BINOL-esters (as hydrobromide **1s** and TFA-salt **1t**, respectively), which gave the same or even better enantioselectivities as achieved with (*S*)-BINOL (**5**) itself. While the proper choice of the solvent is crucial (MeCN), the most significant feature of our investigation is a remarkable anion dependency of enantioselectivity: the hydrobromide **1s** gave 85% ee, whereas the trifluoroacetate **1t** reached 93% ee.

3. Experimental section

3.1. General methods

Preparative column chromatography was carried out using Merck SiO_2 (0.035–0.070 mm, type 60 A) with hexane, ethyl acetate (EA), and *tert*-butylmethylether (MTBE) as eluents. TLC was performed on Merck SiO_2 F_{254} plates on aluminum sheets. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Avance DRX 500. Multiplicities of carbon signals were determined with DEPT experiments. MS and HRMS spectra were obtained with a Finnigan MAT 95 (EI, CI) and a Waters Q-TOF Premier (ESI) spectrometer. IR spectra were recorded on a Bruker Tensor 27 spectrometer equipped with a 'GoldenGate' diamond-ATR unit. Elemental analyses were measured with a Euro EA-CHNS from HEKAtech and optical rotations with a Perkin Elmer polarimeter 343. GLC on a chiral phase was performed with a Focus/Triplus (Thermo Electron) with FID on a column Lipodex E (25 m×0.25 mm) with hydrogen carrier gas (0.4 bar). All starting materials were commercially available.

3.2. (*S*)-2,2′-Bis(1-ethoxyethoxy)-1,1′-binaphthyl (6)

PPTS (219 mg, 0.871 mmol, 0.1 equiv) and EVE (1.88 g, 26.2 mmol, 3 equiv) were added to a suspension of (*S*)-BINOL (2.50 g, 8.70 mmol, 1 equiv) in 15 ml CH_2Cl_2. The resulting light brown mixture was stirred for 16 h at 23 °C. After evaporation of all volatile materials, the crude product was purified by flash chromatography (SiO_2, hexane/EA 5:1, R_f=0.44) to furnish compound **6** (3.54 g, 8.22 mmol, 94%) as pale yellow oil. The ^1H and the $^{13}C\{^1H\}$ NMR spectra showed double signal sets due to three diastereoisomers. ^1H NMR ($CDCl_3$, 500 MHz): δ=0.96 (t, J=7.0 Hz, 6H), 1.05–1.09 (m, 12H), 1.19–1.23 (m, 6H), 3.13–3.21 (m, 2H), 3.24–3.32 (m, 2H), 3.39–3.52 (m, 4H), 5.11 (q, J=5.2 Hz, 2H), 5.21 (q, J=5.2 Hz, 2H), 7.10–7.25 (m, 2×4H), 7.32–7.37 (m, 4H), 7.57–7.60 (m, 2×2H), 7.87 (d, J=8.1 Hz, 2×2H), 7.92 (d, J=9.0 Hz, 2×2H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ=15.02 (2×CH_3), 15.16 (2×CH_3), 20.12 (CH_3), 20.18 (CH_3), 20.21 (CH_3), 20.24 (CH_3), 60.97 (CH_2), 61.00 (CH_2), 61.02 (CH_2), 61.28 (CH_2), 100.38 (CH), 100.53 (CH), 100.77 (CH), 100.85 (CH), 119.26 (CH), 119.45 (CH), 119.77 (CH) 119.85 (CH), 122.16 (C), 122.34 (C), 122.43 (C), 122.54 (C), 123.99 (2×CH), 124.05 (2×CH), 125.67 (CH), 125.70 (CH), 125.74 (CH), 125.77 (CH), 126.11 (CH), 126.12 (CH), 126.15 (CH), 126.18 (CH), 127.79 (4×CH), 129.10 (2×CH), 129.13 (2×CH), 129.83 (CH), 129.93 (CH), 129.96 (CH), 130.01 (CH), 134.07 (C), 134.10 (C), 134.17 (C), 134.23 (C), 152.56 (C–O), 152.61 (C–O), 152.69 (2×C–O) ppm. IR (ATR): $\tilde{\nu}$ = 3059(w), 2978 (m), 2934 (m), 1623 (m), 1594 (m), 1507 (m), 1381 (m), 1329 (m), 1226 (s), 1120 (s), 1074 (s), 977 (s), 946 (s), 865 (s), 809 (s), 751 (s) cm^{-1}. MS (ESI, positive mode), *m*/*z* (%): 437 (100) [M+Li^+], 453 (15) [M+Na^+]. $[\alpha]_D^{20}$ −11.1 (*c* 1.0, $CHCl_3$). $C_{28}H_{30}O_4$ (430.54): calcd C 78.11%, H 7.02%; found C 78.12%, H 7.13%.

3.3. (*S*)-3-Acetyl-2,2′-dihydroxy-1,1′-binaphthyl (7)

n-BuLi (4.7 mmol, 3.0 ml of a 1.6 mol l^{-1} solution in hexanes, 1.2 equiv) was added under an inert atmosphere at 0 °C to a stirred solution of compound **6** (1.7 g, 3.9 mmol, 1 equiv) in abs THF (ca. 8 ml). The resulting mixture was stirred for 15 min at 0 °C and then transferred via a cannula into ice-cold Ac_2O (4.0 g, 39 mmol, 10 equiv). After stirring at 0 °C for 15 min and then at 23 °C for further 15 min, the reaction mixture was poured into 5 ml hydrochloric acid (6 mol l^{-1}). After stirring at 23 °C for another 30 min, the mixture was diluted with CH_2Cl_2 (15 ml). The aqueous layer was extracted with CH_2Cl_2 (2×5 ml). The combined organic layers were washed with H_2O (2×10 ml), satd aqueous solution of $NaHCO_3$ (2×10 ml), and dried over $MgSO_4$. After filtration, the solvent was evaporated and the crude mixture purified by chromatography (SiO_2, hexane/EA 3:1, R_f=0.15). The title compound **7** (499 mg, 1.52 mmol, 39%) was isolated as intense yellow solid, mp 227 °C. Alternatively, the product can be purified by recrystallization from THF/MTBE/hexane (1:3:6). ^1H NMR ($CDCl_3$, 500 MHz): δ=2.89 (s, 3H), 4.97 (s, 1H, OH), 7.06 (d, J=8.4 Hz, 1H, H-8), 7.16–7.19 (m, 1H), 7.23 (ddd, J=1.3, 7.0, 8.3 Hz, 1H), 7.31 (ddd, J=1.0, 7.0, 8.0 Hz, 1H), 7.36 (d, J=9.0 Hz, 1H), 7.38–7.41 (m, 2H), 7.86 (d, J=8.1 Hz, 1H), 7.92 (d, J=8.9 Hz, 1H), 7.94–7.97 (m, 1H), 8.60 (s, 1H), 11.97 (s, 1H, OH) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ=27.02 (CH_3), 113.87 (C), 115.11 (C), 117.72 (CH), 121.23 (C), 123.41 (CH), 124.52 (CH), 124.60 (CH), 124.80 (CH), 126.60 (CH), 127.14 (C), 128.30 (CH), 129.30 (C), 129.97 (CH), 130.26 (CH), 130.63 (CH), 133.43 (C), 134.90 (CH), 137.73 (C), 151.40 (C), 155.65 (C), 204.76 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3343(w), 3054 (w), 2365 (w), 1736 (w), 1619 (s), 1595 (m), 1503 (m), 1430 (m), 1380 (m), 1336 (m), 1312 (s), 1201 (s), 1147 (m), 1079 (m), 957 (m), 935 (m), 897 (m), 814 (m), 745 (s), 703 (m) cm^{-1}. HRMS (CI, *iso*-butane): found 329.1178 [M+H^+], calcd 329.1178 (for $C_{22}H_{17}O_3$). $[\alpha]_D^{20}$ −33.0 (*c* 1.0, $CHCl_3$). $C_{22}H_{16}O_3$ (328.11).

3.4. (*S,S*)-2-(3′-Acetyl-2′-hydroxy-1,1′-binaphthyl-2-yl) 1-benzyl pyrrolidine-1,2-dicarboxylate (1k)

DCC (173 mg, 800 μmol, 1.2 equiv) was added at 0 °C to a mixture of *N*-Cbz-L-proline (**4k**) (181 mg, 700 μmol, 1 equiv) and DMAP (8.6 mg, 70 μmol, 0.1 equiv) in 2 ml CH_2Cl_2. The solution was stirred about 5 min, until a white solid precipitated. A solution of compound **7** (230 mg, 700 μmol, 1 equiv) in 5 ml CH_2Cl_2 was added and the resulting mixture was stirred for 16 h at 60 °C. After filtration, the organic layer was washed successively with a satd aqueous solution of NH_4Cl (3×10 ml), satd aqueous solution of $NaHCO_3$ (3×10 ml), and H_2O (3×10 ml). After drying over $MgSO_4$, filtration and evaporation of volatile materials the crude mixture was purified by chromatography (SiO_2, hexane/MTBE 1:2, R_f=0.21) to yield the title compound **1k** (325 mg, 581 μmol, 83%) as an intense yellow solid, mp 78 °C. The ^1H and the $^{13}C\{^1H\}$ NMR spectra showed partly doubled signal sets due to *E*/*Z* isomers of the amide and carbamate moieties. ^1H NMR ($CDCl_3$, 500 MHz): δ=1.30–1.71 (m, 4H), 2.79 (s, 3H, CH_3), 3.15–3.23 (m, 2H), 4.09–4.18 (m, 1H), 4.93–5.08 (m, 2H), 6.93–6.96 (m, 1H), 7.18–7.45 (m, 11H), 7.81–7.90 (m, 3H), 8.44–8.46 (m, 1H), 11.63–11.65 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ=22.80 (CH_2), 23.63 (CH_2), 25.54 ($2CH_2$), 26.90 ($2CH_2$), 28.90 (CH_3), 29.89 (CH_2), 46.10 (CH_2), 46.58 (CH_2), 58.63 (CH), 59.16 (CH), 66.82 (CH_2), 66.88 (CH_2), 116.86 (C), 117.08 (C), 120.78 (C), 120.87 (C), 121.39 (CH), 121.89 (CH), 123.39 (C), 123.52 (C), 124.15 (CH), 124.19 (CH), 124.91 (2CH), 125.11 (2CH), 125.54 (2CH), 125.62 (2CH), 126.54 (CH), 126.58 (C), 126.63 (CH), 127.63 (2CH), 127.81 (CH), 127.84 (CH), 127.88 (2CH), 128.20 (CH), 128.27 (CH), 128.36 (2CH), 128.43 (2CH), 129.41 (CH), 129.45 (2CH), 129.50 (CH), 129.97 (2CH), 130.06 (CH), 131.83 (C), 131.88 (C), 133.18 (C), 133.81 (2CH), 136.56 (C), 136.64 (C), 137.27 (C), 137.42 (C), 146.57 (C–O), 146.85 (C–O), 153.89 (C–O), 154.67 (C=O), 154.74 (C=O), 170.33 (C=O), 204.57 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3508(w), 2931 (w), 2814 (w), 1763 (m), 1702 (s), 1643 (s), 1607 (w), 1502 (w), 1411 (s), 1342 (s), 1306 (s), 1254 (w), 1206 (m), 1143 (s), 1130 (s), 1081 (m), 1038 (w), 1022 (w), 959 (w), 909 (w), 856 (w), 808 (w), 790 (w), 748

(m), 697 (m), 647 (w) cm^{-1}. HRMS (EI, 70 eV): found 559.1995 [M^+], calcd 559.2001 (for $C_{35}H_{29}NO_6$). $[\alpha]_D^{20}$ −82.7 (*c* 1.0, THF). $C_{35}H_{29}NO_6$ (559.20): calcd. C 75.12%, H 5.22%, N 2.50%; found C 74.86%, H 5.62%, N 2.48%.

3.5. (*S*,*S*)-2-[(3′-Acetyl-2′-hydroxy-1,1′-binaphthyl-2-yl) oxycarbonyl]pyrrolidiniumbromide (1s)

A solution of HBr in AcOH (590 mg, 2.40 mmol, 33% w/w, 4 equiv) was added to compound **1k** (330 mg, 590 μmol, 1 equiv) under an inert atmosphere. The resulting dark red mixture was stirred until TLC showed complete conversion (ca. 30–45 min). Abs Et_2O (1 ml) was added under vigorous stirring and a solid precipitated. The supernatant was removed via syringe. After repetition with another 1 ml of abs. Et_2O, the resulting crude product was washed with *n*-hexane (3×1 ml) and dried under reduced pressure. The title compound **1s** (253 mg, 500 μmol, 85%) was isolated as brown solid, mp 129 °C. ^1H NMR (DMSO-d_6, 500 MHz): δ=0.87–0.90 (m, 1H), 1.27–1.30 (m, 1H), 1.51–1.63 (m, 2H), 2.30–2.80 (m, 2H), 2.93 (s, 3H), 4.24–4.15 (m, 1H), 6.80–6.90 (m, 1H), 7.31 (d, *J*=7.1 Hz, 1H), 7.44–7.54 (m, 3H), 7.56–7.65 (m, 2H), 8.09–8.25 (m, 3H), 9.04 (s, 1H), 9.5–10.2 (br s, 2H), 11.79 (s, 1H, OH) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ=25.89 (CH_2), 28.44 (CH_3), 31.79 (CH_2), 52.08 (CH_2), 62.55 (CH), 116.18 (C), 121.69 (CH), 123.72 (C), 123.91 (CH), 125.20 (CH), 125.81 (CH), 126.47 (CH), 126.96 (C), 127.54 (CH), 128.96 (CH), 129.19 (CH), 129.66 (CH), 131.32 (CH), 132.94 (C), 132.97 (C), 133.34 (CH), 137.31 (C), 139.47 (C), 145.99 (C–O), 154.84 (C–O), 167.64 (C=O), 205.72 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 2926(w), 2713 (w), 1760 (m) 1643 (m), 1606 (w), 1575 (w), 1503 (w), 1431 (w), 1341 (m), 1305 (m), 1205 (s), 1080 (w), 1038 (w), 1021 (w), 958 (w), 940 (w), 894 (w), 811 (w), 790 (w), 747 (s), 704 (m), 627 (w) cm^{-1}. HRMS (EI, 70 eV): found 426.1681 [$M-Br^-$], calcd 426.1700 (for $C_{27}H_{24}NO_4$). $[\alpha]_D^{20}$ −100.1 (*c* 1, $CHCl_3$). $C_{27}H_{24}BrNO_4$ (505.09).

3.6. (*S*,*S*)-2-[(3′-Acetyl-2′-hydroxy-1,1′-binaphthyl-2-yl) oxycarbonyl]pyrrolidiniumtrifluoroacetate (1t)

Compound **1s** (90 mg, 18 μmol) was stirred with excess (2.5 ml) TFA at 23 °C for 12 h. After evaporation of all volatile materials, title compound **1t** (94 mg, 0.17 mmol, 96%) was obtained as light brown solid, mp 97 °C. ^1H NMR (DMSO-d_6, 500 MHz): δ=0.86–0.88 (m, 1H), 1.29–1.31 (m, 1H), 1.51–1.63 (m, 2H), 2.93 (s, 3H), 2.99–3.07 (m, 2H), 4.34–4.38 (m, 1H), 6.89–6.93 (m, 1H), 7.20 (d, *J*=7.2 Hz, 1H), 7.44–7.54 (m, 3H), 7.56–7.65 (m, 2H), 8.09–8.25 (m, 3H), 9.04 (s, 1H), 9.5–10.2 (br s, 2H), 11.77 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ=23.88 (CH_2), 28.34 (CH_3), 30.87 (CH_2), 47.10 (CH_2), 59.83 (CH), 115.68 (C), 120.75 (C), 121.28 (CH), 123.53 (C), 124.45 (CH), 124.58 (CH), 125.86 (CH), 126.16 (CH), 126.45 (C), 126.93 (CH), 128.38 (CH), 130.17 (CH), 130.22 (CH), 130.46 (CH), 131.96 (C), 132.79 (C), 135.09 (CH), 136.76 (C), 145.53 (C–O), 154.37 (C–O), 167.23 (C=O), 205.08 (C=O) ppm. $^{19}F\{^1H\}$ NMR ($CDCl_3$, 470 MHz): δ=−75.5 ppm. IR (ATR): $\tilde{\nu}$ = 2926(w), 2714 (w), 1761 (m), 1644 (m), 1607 (w), 1577 (w), 1504 (w), 1452 (w), 1432 (w), 1342 (m), 1306 (m), 1202 (s), 1081 (w), 1038 (w), 1022 (w), 958 (w), 940 (w), 919 (w), 894 (w), 811 (w), 792 (w), 748 (s), 704 (m), 628 (w) cm^{-1}. MS (ESI, positive mode), *m*/*z* (%): 426 (100) [$M-CF_3COO^-$], 448 (6) [$M-CF_3COOH+Na^+$], 466 (15) [$M-CF_3COOH+K^+$]. MS (ESI, negative mode), *m*/*z* (%): 69 (35) [CF_3^-], 113 (100) [CF_3COO^-]. HRMS (EI, 70 eV): found 426.1694 [$M-CF_3COO^-$], calcd 426.1700 (for $C_{27}H_{24}NO_4$). $[\alpha]_D^{20}$ −140.7 (*c* 1.5, $CHCl_3$). $C_{29}H_{24}F_3NO_6$ (539.16).

Acknowledgements

We are grateful to Anike Nörder for initial experiments and to Katrin Elberfeld for supporting us in the laboratory.

References and notes

1. Review: (a) Mehrotra, R. C. *Pure Appl. Chem.* **1988**, *60*, 1349–1356; (b) Christoffers, J.; Frey, H. *Chim. Oggi/Chem. Today Suppl.* **2008**, *26*, 26–28.
2. (a) Bocknack, B. M.; Wang, L.-C.; Hughes, F. W.; Krische, M. J. *Tetrahedron* **2005**, *61*, 6266–6275; (b) Albrecht, M.; Dehn, S.; Raabe, G.; Fröhlich, R. *Chem. Commun.* **2005**, 5690–5692; (c) Albrecht, M.; Dehn, S.; Schmid, S.; De Groot, M. *Synthesis* **2007**, 155–158; (d) Albrecht, M.; Schmid, S.; Dehn, S.; Wickleder, C.; Zhang, S.; Bassett, A. P.; Pikramenou, Z.; Fröhlich, R. *New J. Chem.* **2007**, *31*, 1755–1762.
3. Reviews: (a) Chen, Y.; Yeka, S.; Yudin, A. K. *Chem. Rev.* **2003**, *103*, 3155–3211; (b) Au-Yeung, T. T.-L.; Chan, S.-S.; Chan, A. S. C. *Adv. Synth. Catal.* **2003**, *345*, 537–555; (c) Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857–897.
4. (a) Carreira, E. M.; Singer, R. A.; Lee, W. *J. Am. Chem. Soc.* **1994**, *116*, 8837–8838; (b) Saha, S.; Moorthy, J. N. *Tetrahedron Lett.* **2010**, *51*, 912–916; (c) Review: Frantz, D. E.; Fässler, R.; Tomooka, C. S.; Carreira, E. M. *Acc. Chem. Res.* **2000**, *33*, 373–381.
5. (a) Shen, X.; Guo, H.; Ding, K. *Tetrahedron: Asymmetry* **2000**, *11*, 4321–4327; (b) Nakamura, Y.; Takeuchi, S.; Okumura, K.; Ohgo, Y.; Curran, D. P. *Tetrahedron* **2002**, *58*, 3963–3969; (c) Harada, T.; Kanda, K. *Org. Lett.* **2006**, *8*, 3817–3819; (d) Ma, L.; Jin, R.-Z.; Lü, G.-H.; Bian, Z.; Ding, M.-X.; Gao, L.-X. *Synthesis* **2007**, 2461–2470; (e) Abreu, A. R.; Pereira, M. M.; Bayon, J. C. *Tetrahedron* **2010**, *66*, 743–749; (f) Review: Walsh, P. J. *Acc. Chem. Res.* **2003**, *36*, 739–749.
6. Mori, M.; Nakai, T. *Tetrahedron Lett.* **1997**, *38*, 6233–6236.
7. Review: Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem.* **2004**, *116*, 2256–2276; *Angew. Chem., Int. Ed.* **2004**, *43*, 2206–2225.
8. Buisman, G. J. H.; van der Veen, L. A.; Klootwijk, A.; de Lange, W. G. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. *Organometallics* **1997**, *16*, 2929–2939.
9. Würdemann, M.; Christoffers, J. *Org. Biomol. Chem.* **2010**, *8*, 1894–1898.
10. Ben-Ishai, D.; Berger, A. *J. Org. Chem.* **1952**, *17*, 1564–1570.
11. (a) Zhang, F.-Y.; Yip, C.-W.; Cao, R.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 585–589; (b) Balsells, J.; Davis, T. J.; Carroll, P.; Walsh, P. J. *J. Am. Chem. Soc.* **2003**, *124*, 10336–10348.
12. (a) Allred, E. A.; Sonnenberg, J.; Winstein, S. *J. Org. Chem.* **1960**, *25*, 26–29; (b) Mao, J.; Wan, B.; Wang, R.; Wu, F.; Lu, S. *J. Org. Chem.* **2004**, *69*, 9123–9127.
13. Budhram, R. S.; Palaniswamy, V. A.; Eisenbraun, E. J. *J. Org. Chem.* **1986**, *51*, 1402–1406.
14. Xu, J.; Wei, T.; Zhang, Q. *J. Org. Chem.* **2004**, *69*, 6860–6866.
15. (a) Hatano, M.; Miyamoto, T.; Ishihara, K. *J. Org. Chem.* **2006**, *71*, 6474–6484; (b) Hatano, M.; Miyamoto, T.; Ishihara, K. *Adv. Synth. Catal.* **2005**, *347*, 1561–1568.